(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
1 September 2005 (01.09.2005)

PCT

(10) International Publication Number
WO 2005/079745 A1

(51) International Patent Classification[7]: A61K 7/48

(21) International Application Number:
PCT/GB2005/000503

(22) International Filing Date: 19 February 2005 (19.02.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0403702.4 19 February 2004 (19.02.2004) GB
0419260.5 31 August 2004 (31.08.2004) GB

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Declaration under Rule 4.17:**
— *of inventorship (Rule 4.17(iv)) for US only*

**Published:**
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: SKINCARE COMPOSITIONS COMPRISING SALICYLIC ACID

(57) Abstract: There is disclosed a skincare composition suitable for topical application to the skin. The composition comprises salicylic acid or a salt thereof and hydrolysed milk protein. The composition is useful in the treatment of acne.

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# SKINCARE COMPOSITIONS COMPRISING SALICYLIC ACID

This invention relates to skincare compositions, in particular compositions effective in the treatment of acne vulgaris, and to methods of treatment of the skin that involve the application of such compositions.

Acne vulgaris (acne) is a chronic inflammatory condition of the pilosebaceous units of the skin, which is particularly prevalent in adolescents. The condition generally causes the formation, on the skin, of comedones, red papules, pustules and sometimes cysts. This is unsightly and furthermore, if untreated, acne can lead to scarring of the skin. The major causes of acne are thought to be an increase in sebum production, an increased presence of *propionibacterium acne* (*P. acne*), blockage of the pilosebaceus duct and the production of inflammation.

Salicylic acid is known to be effective in the treatment of acne. It is a topical keratolytic agent that works by dissolving the intercellular cement that holds epithelial cells together. Salicylic acid is used in a variety of over-the-counter acne remedies.

In order to improve the efficacy of topical acne treatments, it is desired to formulate salicylic acid with one or more oil control agents such as sebum regulators which regulate the number of active glands or oil absorbing agents which remove excess oil from the skin. In order to ensure optimum performance, it is necessary to suspend the oil control agents in the skincare composition. However, a problem arises when producing such formulations as the ingredients necessary to suspend the oil control agents are less stable at the acidic pH of the salicylic acid compositions and satisfactory suspensions may not be formed. For example, using carbomer (trade name

Carbopol, available from B.F. Goodrich) as the thickener in an aqueous carrier, it was found that combining salicylic acid with oil control agents such as talc, charcoal, rice starch and clay led to compositions which did not maintain the oil control agent in suspension for a satisfactory period. Similar results were also obtained with thickeners such as Acrylates/Palmeth-25 Acrylate copolymer (available from 3V Sigma S.P.A under the trade name Synthalen W2000) and xanthan gum (available from Kelco under the trade name Keltrol RD). In addition, it was found that incorporating sebum regulators such as Algae Extract, Burdock Extract, Watercress Extract and Orange extract into salicylic acid compositions led to compositions which were unable to form an acceptable hydro-lipid film on the skin. The formation of an acceptable hydro-lipid film on the skin is important to restore the equilibrium of all skin types by normalising the sebum flow through controlling the production of the sebum and regulating the number of effective glands.

Surprisingly, it has now been found that skincare compositions comprising salicylic acid and hydrolysed milk protein have improved therapeutic efficacy in the treatment of acne. Said skincare compositions have both the ability to treat acne and establish a normal hydro-lipid film on the skin.

Hydrolysed milk protein is the hydrolysate of milk protein derived by acid, enzyme or other method of hydrolysis. Hydrolysed milk protein has previously been known for use to condition hair and skin. It may be used as a sebum regulator to restore the flow of sebum in dry skin and reduce excessive production of sebum in oily skin. It has not previously been employed as an active agent in the treatment of acne. However, in view of the results obtained with other oil control agents, it is surprising that hydrolysed milk protein in combination with salicylic acid has such a marked effect. For example, it has been shown that stable suspensions can be

formed even at acid pH. Furthermore, trials have shown that even after a single application, both rinse-off and leave-on products cause the sebum level to be reduced for at least six hours. In addition, trials show a delay in the re-greasing of the skin and the achievement of significant reduction in the production of sebum even after a few days, for example three days, even with compositions that are rinsed off after application. With this combination, effective treatment of acne can be achieved as it is possible to restore the equilibrium of all skin types by normalising the sebum flow through controlling the production of the sebum and regulating the number of effective glands, even taking into account the over-drying and irritating effects of salicylic acid on the skin. Studies have also demonstrated that compositions containing a combination of salicylic acid and hydrolysed milk protein allow salicylic acid to penetrate deep into the pores, salicylic acid can even be detected in the pilosebaceous ducts. With repeated applications, salicylic acid can still be detected in the pores after up to eight hours, even when the product is rinsed off. Furthermore, the salicylic acid compositions are found to be well tolerated by the skin. This is particularly important as salicylic acid compositions can cause some degree of local skin peeling and discomfort such as burning and skin reddening.

Thus, according to a first aspect of the invention there is provided a skincare composition suitable for topical application to the skin, said composition comprising salicylic acid or a salt thereof and hydrolysed milk protein.

Salicylic acid is preferably incorporated into the composition according to the invention as the free acid. However, the pH of the composition may, and generally will, be such that the salicylic acid exists in the composition in dissociated form. As the composition may well contain cationic counterions, the salicylic acid may then be thought of as being present in salt form. Alternatively, the salicylic acid may be incorporated into the composition in

salt form, eg as a salt with a Group I metal, such as sodium salicylate. As used herein, unless the context requires otherwise, any and all references to salicylic acid should be taken to encompass references to the acid and to dissociated forms and salts thereof.

The concentration of salicylic acid in the composition according to the invention is preferably at least 0.01% by weight, more preferably at least 0.1%, most preferably at least 0.5% and especially at least 1% by weight. The concentration of salicylic acid is preferably less than 10%, more preferably less than 5%, most preferably less than 4% and especially less than 3% by weight. The concentration of salicylic acid may therefore fall in the range 0.01% to 10% by weight, more preferably 0.1% to 5%, and most preferably 0.5% to 4% and especially 1 to 3% by weight. A particularly preferred concentration of salicylic acid is 2% by weight.

The concentration of hydrolysed milk protein in the composition according to the invention is preferably at least 0.01% by weight, more preferably at least 0.05% by weight, most preferably at least 0.08% by weight and especially at least 0.1% by weight. The concentration of hydrolysed milk protein is preferably less than 10%, more preferably less than 3%, most preferably less than 2% and especially less than 1% by weight. The concentration of hydrolysed milk protein may therefore fall within the range 0.01% to 10% by weight, more preferably 0.05% to 3%, most preferably 0.08% to 2% and especially 0.1 to 1.0% by weight. A particularly preferred concentration of hydrolysed milk protein is 0.2% by weight.

In preferred compositions according to the present invention, the concentration of salicylic acid is in the range from 0.5 to 4% by weight, more preferably from 0.5 to 2% by weight and the concentration of hydrolysed milk protein is in the range from 0.08 to 2%, more preferably from 0.1 to 0.5 % by

weight. In further preferred compositions, the ratio of salicylic acid or salt thereof to hydrolysed milk protein is in the range from 1:1 to 20:1 parts by weight, more preferably from 2:1 to 15:1 parts by weight, most preferably from 5:1 to 12:1 parts by weight.

The composition is preferably prepared with a pH in the range 2.3 to 7.0, more preferably 2.5 to 6.0, and particularly a pH in the range 2.5 to 4.0, eg about pH 3.0 or pH 3.5.

A composition according to the invention may comprise salicylic acid (or salt thereof) and hydrolysed milk protein as the sole active ingredients. However, a composition according to the invention may comprise one or more further topically active ingredients useful in skincare. Such active ingredients may include one or more of the following:

antimicrobial or antibacterial compounds, for example selected from the following:
triclosan, neomycin, clindamycin, polymyxin, bacitracin, benzoyl peroxide, hydrogen peroxide, tetracylines such as doxycycline or minocycline, sulfa drugs such as sulfacetamide, penicillins, cephalosporins such as cephalexin, and quinolones such as lomefloxacin, olfoxacin or trovafloxacin;

antiviral compounds, for example selected from acyclovir, tamvir, and penciclovir;

antifungal compounds, for example selected from the following: farnesol, clotrimazole, ketoconazole, econazole, fluconazole, calcium or zinc undecylenate, undecylenic acid, butenafine hydrochloride, ciclopirox olaimine, miconazole nitrate, nystatin, sulconazole, and terbinafine hydrochloride;

anti-inflammatory compounds, for example selected from the following: steroidal agents selected from hydrocortisone, fluocinolone acetonide, halcinonide, halobetasol propionate, clobetasol propionate, betamethasone dipropionate, betamethasone valerate, and triamcinolone acetonide, and non-steroidal anti-inflammatory agents selected from aspirin, ibuprofen, ketoprofen, naproxen, aloe vera gel, aloe vera, licorice extract, pilewort, Canadian willow root, zinc, and allantoin;

anthelmintic compounds, for example metronidazole.

Particularly suitable antibacterial agents are peroxide antibacterial agents. A preferred peroxide antibacterial agent for inclusion in the composition is hydrogen peroxide. Alternatively, the composition may comprise a compound that, in use, is capable of generating hydrogen peroxide. An example of the latter class of compound is an adduct such as urea peroxide (carbamide peroxide).

In one preferred embodiment of the invention, the composition comprises a combination of salicylic acid, hydrolysed milk protein and hydrogen peroxide.

Where hydrogen peroxide is present in the composition according to the invention, the concentration of hydrogen peroxide is preferably at least 1% by weight. The concentration of hydrogen peroxide is preferably less than 5%, more preferably less than 3%, and most preferably less than 2%. The concentration of hydrogen peroxide may therefore fall within the range 1% to 5% by weight, more preferably 1% to 3%, and most preferably 1% to 2%.

The composition according to the invention may also comprise one or more ingredients which have a cooling effect on the skin, for example volatile ingredients, such as menthol.

The composition according to the invention may be formulated in numerous forms. However, the composition may often take the form of an aqueous or oily solution or dispersion or emulsion or a gel. An emulsion may be an oil-in-water emulsion or a water-in-oil emulsion.

The oil phase of water-in-oil or oil-in-water emulsions may comprise for example:

a) hydrocarbon oils such as paraffin or mineral oils;
b) waxes such as beeswax or paraffin wax;
c) natural oils such as sunflower oil, apricot kernel oil, shea butter or jojoba oil;
d) silicone oils such as dimethicone, cyclomethicone or cetyldimethicone;
e) fatty acid esters such as isopropyl palmitate, isopropyl myristate, dioctylmaleate, glyceryl oleate and cetostearyl isononanoate;
f) fatty alcohols such as cetyl alcohol or stearyl alcohol and mixtures thereof (eg cetearyl alcohol);
g) polypropylene glycol or polyethylene glycol ethers, eg PPG-14 butyl ether; or
h) mixtures thereof, for example, the blend of waxes available commercially under the trade name Cutina (Henkel).

Emulsifiers used may be any emulsifiers known in the art for use in water-in-oil or oil-in-water emulsions. Known cosmetically acceptable emulsifiers include:

a) sesquioleates such as sorbitan sesquioleate, available commercially for example under the trade name Arlacel 83 (ICI), or polyglyceryl-2-sesquioleate;

b) ethoxylated esters of derivatives of natural oils such as the polyethoxylated ester of hydrogenated castor oil available commercially for example under the trade name Arlacel 989 (ICI);

c) silicone emulsifiers such as silicone polyols available commercially for example under the trade name ABIL WS08 (Th. Goldschmidt AG);

d) anionic emulsifiers such as fatty acid soaps e.g. potassium stearate and fatty acid sulphates e.g. sodium cetostearyl sulphate available commercially under the trade name Dehydag (Henkel);

e) ethoxylated fatty alcohols, for example the emulsifiers available commercially under the trade name Brij (ICI);

f) sorbitan esters, for example the emulsifiers available commercially under the trade name Span (ICI);

g) ethoxylated sorbitan esters, for example the emulsifiers available commercially under the trade name Tween (ICI);

h) ethoxylated fatty acid esters such as ethoxylated stearates, for example the emulsifiers available commercially under the trade name Myrj (ICI);

i) ethoxylated mono-, di-, and tri-glycerides, for example the emulsifiers available commercially under the trade name Labrafil (Alfa Chem.);

j) non-ionic self-emulsifying waxes, for example the wax available commercially under the trade name Polawax (Croda);

k) ethoxylated fatty acids, for example, the emulsifiers available commercially under the trade name Tefose (Alfa Chem.);

l) methylglucose esters such as polyglycerol-3 methyl glucose distearate available commercially under the name Tegocare 450 ( Degussa Goldschmidt); or

m) mixtures thereof.

Gels provided according to the invention may be aqueous or non-aqueous. Aqueous gels are preferred. The gel will contain a gelling agents in order to give sufficient viscosity to the gel. A particularly suitable gelling agent is a copolymer of acryloyl dimethyl tauric acid (or a salt thereof), especially a copolymer of that monomer with another vinylic monomer. The salt may be a salt of a Group I alkali metal, but is more preferably an ammonium salt. Examples of suitable copolymer gelling agents are ammonium acryloyl dimethyl taurate / vinyl pyrrolidone copolymer, ammonium acryloyl dimethyl taurate / Beheneth-25 methacrylate copolymer, ammonium acryloyldimethyltaurate / vinyl formamide copolymer, These materials are available from Clariant GmbH in the range of products under the trade name Aristoflex.

A variety of thickening agents may also be used according to the nature of the liquid carrier and the viscosity required. Thickeners that are water-soluble or hydrophilic are preferred, and examples include acrylic acid polymers, eg those available commercially under the trade name Carbopol (B.F. Goodrich), modified celluloses, eg hydroxypropylmethylcellulose or hydroxyethylcellulose available commercially under the trade name Natrosol (Hercules), alkylgalactomanans available under the trade name N-Hance, xanthan gum, cetyl alcohol and sodium chloride.

The amount of gelling and/or thickening agent in the composition will each preferably lie in the range 0.1 to 5% w/w, more preferably 0.5 to 5% w/w. Typically, the amount of gelling and/or thickening agent will each be less than 3% w/w, eg about 1% w/w or about 2% w/w.

The composition according to the invention preferably has a viscosity of from about 50 mPa.s to about 20,000 mPa.s, more preferably from about 100 mPa.s to about 10,000 mPa.s. Viscosity may be measured using a

Brookfield RVT viscometer equipped with a spindle 4 rotating at 10rpm after 2 minutes.

In many instances, it is preferred that the composition should comprise a chelating or sequestering agent, or other agent capable of complexation or other interaction with metal ions present in the composition. Such agents may improve the stability of the composition, and in particular may inhibit or prevent degradation of several ingredients (eg fragrance). Examples of chelating or sequestering agents include ethylenediamine tetraacetic acid and its salts, notably the dipotassium and especially the disodium salt.

In the case of solutions or dispersions, and gels, the composition will generally contain a solvent system or other continuous liquid phase. Such a system is preferably aqueous. However, mixed solvent systems may often be used with advantage. Such a mixed solvent system most preferably comprises water, in admixture with a co-solvent, most preferably a lower (eg $C_{1-6}$) alcohol, in particular ethanol and t-butyl alcohol.

Preferred aqueous systems comprise water in an amount of at least 50% by weight, more preferably at least 60% by weight, most preferably at least 70% by weight and especially at least 80% by weight. The upper limit of water will depend on the amounts of other ingredients incorporated in the composition so that the water may form the remainder of the composition up to 100% of the composition. A typical maximum value is less than 90% by weight, for example 80% by weight or 85% by weight.

The composition most preferably comprises in excess of 5% w/w of the cosolvent, and may comprise in excess of 10% w/w, in excess of 20% w/w, or in excess of 30% w/w of the cosolvent. The amount of cosolvent present in the composition preferably does not exceed 50% w/w. The amount of

cosolvent thus preferably lies in the range 5% to 50% w/w, more preferably 10% to 50% w/w. In general, higher proportions of cosolvent may be required in compositions containing higher proportions of ingredients (eg topically active ingredients, as discussed above) that are of low solubility in water. Where such ingredients are absent, of their concentration is relatively low, the proportion of cosolvent may also be somewhat lower than in other embodiments, eg up to 20% w/w.

The composition may additionally comprise other components which will be well known to those skilled in the art. These include, for example:

a) Emollients – ingredients that help to maintain the soft, smooth and pliable appearance of skin. Such ingredients may function by their ability to remain on the surface of the skin or in the stratum corneum, and to act as lubricants, reducing or preventing flaking of the skin and improving the skin's appearance. Examples of emollients are isopropyl myristate, triglycerides of fatty acids eg lauric triglyceride or capric/caprylic triglyceride, such as the triglyceride available commercially under the trade name Miglyol 810 (Huls UK), and the polypropylene glycol ether of stearyl alcohol known as PPF-15 Stearyl Ether. Particularly preferred emollients are polysiloxane compounds, in particular those known as cyclomethicone, ie cyclic dimethyl polysiloxane compounds that conform to the formula:

$$-(Si(CH_3)_2)_n-$$

in which n has a value between 3 and 7.

b) Humectants or Moisturisers – ingredients intended to increase the water content of the top layers of the skin. Examples of such ingredients are glycerin, 1,3-butylene glycol and propylene glycol.

c) Surfactants – Surfactants may be used in compositions according to the invention as solubilisers, or as cleansing agents or foam boosters. Many different classes of surfactant may be suitable for inclusion in the composition according to the invention, and these will be readily apparent to those skilled in the art. Examples of suitable surfactants include polyethylene glycol ethers of alcohols such as isocetyl alcohol (eg Isoceteth-20), isostearyl alcohol (eg Isosteareth-20), cetyl alcohol (eg Ceteth-20), oleyl alcohol (eg Oleth-20) and cetearyl alcohol (eg Ceteareth-20). A particularly preferred surfactant for use in the invention is Isoceteth-20.

d) Emulsion stabilising salts such as sodium chloride, sodium citrate or magnesium sulphate.

e) Preservatives – ingredients which prevent or retard microbial growth and thus protect the composition from spoilage. Examples of preservatives include such as propylparaben, bronopol, sodium dehydroacetate, polyhexamethylenebiguanide hydrochloride, isothiazolone and diazolidinylurea.

f) Chelating agents or sequestering agents (sequestrants) – ingredients that have the ability to complex with and inactivate metallic ions in order to prevent their adverse effects on the stability or appearance of the composition, as described above. Examples of chelating agents are ethylenediamine tetraacetic acid and its salts, notably the dipotassium and especially the disodium or tetrasodium salt.

g) Abrasives – ingredients used to assist in the removal of unwanted tissue or foreign materials from the skin during application of the composition. Abrasives commonly comprise fine solid particles. One example of a suitable abrasive is polyethylene beads.

h) pH adjusters – Ingredients used to control the pH of the composition. Examples of pH adjusters are inorganic salts such as sodium hydroxide, and organic bases such as triethanolamine.

i) Conditioning agents, for example distearyldimonium chloride.

j) Perfumes and colourings.

The composition according to the invention may be applied and left on the skin to have the desired therapeutic effect or it may be applied and then rinsed off, for example with water. The composition may be applied with the aid of a fibrous material, for example a pad or a wipe.

According to another aspect of the invention, there is provided an article comprising a fibrous substrate, for example a material in the form of a pad or a wipe, impregnated with a skincare composition comprising salicylic acid or a salt thereof and hydrolysed milk protein. The fibrous material may be used to apply the composition onto the skin.

Preferably, said fibrous material is impregnated with the skincare composition according to the inventionin an amount in the range from 10 to 30% by weight, preferably from 15 to 25% by weight and most preferably from 18 to 22% by weight of the fibrous material. Suitable fibrous materials include cellulose or cotton fibres or a mixture thereof. The fibrous material may be impregnated with the composition as a wet wipe which is arranged for immediate use to

apply the skincare composition of the present invention to the skin of the user. Alternatively, the fibrous material may be impregnated with the skincare composition and dried to form a dry wipe which requires to be wetted, for example with water, before it can be used.

According to a further aspect of the invention, there is provided method for the prophylactic or remedial treatment of acne, which method comprises the topical application to the skin of a patient of a skincare composition comprising salicylic acid or a salt thereof and hydrolysed milk protein.

It will be appreciated that the method according to this aspect of the invention may be a therapeutic method, but will often be a primarily cosmetic method, the objective of which is to reduce or eliminate externally visible, and often unsightly, symptoms of acne vulgaris.

In a yet further aspect of the invention, there is provided the use of salicylic acid and hydrolysed milk protein in the manufacture of a composition for the prophylactic or remedial treatment of acne by topical application of the composition to the skin.

The invention will now be described in greater detail, by way of illustration only, with reference to the following Examples. In the Examples the hydrolysed milk protein is obtained from Sederma, France; the spunlace is obtained from Jacob Holm Industries (France) under the trade name Standard JH50gsm Spunlace JH501074L2.

Example 1

Oil Control Cream Wash

| Ingredients | %w/w |
|---|---|
| Sodium cocoyl isethionate | 16.40 |
| Cetyl alcohol | 10.00 |
| Laureth-3 | 5.00 |
| Glycerin | 3.00 |
| Salicylic acid | 2.00 |
| Sodium hydroxide | 0.36 |
| Hydrolysed Milk Protein | 0.20 |
| Parfum | 0.20 |
| Disodium EDTA | 0.01 |
| Aqua | to 100% |

Method

The cetyl alcohol and laureth-3 were heated to 60°C to form the oil phase. The remainder of the ingredients were mixed to form the aqueous phase. The oil phase was added to the aqueous phase. The composition was cooled down to room temperature with stirring to form a uniform composition.

Example 2

Scrub Wipe

| Ingredients | %w/w |
|---|---|
| PPG-14 butyl ether | 8.00 |
| Cetearyl isononoate | 2.25 |
| Salicylic acid | 2.00 |
| Ceteareth-20 | 1.13 |

| | |
|---|---|
| Cetearyl alcohol | 1.13 |
| Glyceryl Stearate | 0.45 |
| Glycerin | 0.45 |
| Hydrolysed Milk Protein | 0.20 |
| Hydrogen peroxide (active 35%) | 1.50 |
| Menthol | 0.10 |
| Disodium EDTA | 0.10 |
| Cetyl palmitate | 0.15 |
| Ceteareth palmitate | 0.15 |
| Parfum | 0.10 |
| Aqua | to 100% |

Method

All the ingredients, apart from hydrolysed milk protein, hydrogen peroxide, menthol and parfum, were mixed and heated to 90°C. The mixture was cooled down to room temperature with stirring. The remaining ingredients were stirred into the mixture to form a uniform composition.

The mixture was impregnated into a wipe material available as Standard Spunlace , width 895mm-1074mm, thickness 0.55mm, absorption capacity 1091%, basic weight 50.7g/m2,using 140ml lotion to 32 wipes.

Example 3

Gel Wash

| Ingredients | %w/w |
|---|---|
| Laureth sulphate | 11.9 |
| Coco glucoside | 4.0 |
| Glycerin | 3.0 |

| | |
|---|---|
| Salicylic acid | 2.0 |
| Sodium chloride | 1.6 |
| Hydrolysed Milk Protein | 0.2 |
| Parfum | 0.2 |
| Menthol | 0.1 |
| Aqua | to 100% |

Method

All the ingredients were mixed at room temperature to form a uniform composition.

Example 4

Lotion for Impregnated Pads

| Ingredients | %w/w |
|---|---|
| Alcohol(99.9%) and t-Butylalcohol(0.1%) | 37.00 |
| Isoceteth-20 | 3.00 |
| Salicylic acid | 2.00 |
| Hydrogen Peroxide (active 35%) | 4.29 |
| Hydrolysed Milk Protein (mixed with propylene glycol and water) | 0.20 |
| Sodium hydroxide (30%) | 0.20 |
| Parfum | 0.10 |
| Disodium EDTA | 0.005 |
| Aqua | to 100% |

Method

All the ingredients were mixed at room temperature to form a uniform composition. The composition was impregnated into a non-woven pad

consisting of rayon and polypropylene using approximately 100ml lotion for 65 pads.

Example 5

Cream Scrub

| Ingredients | %w/w |
|---|---|
| Stearyl alcohol | 3.00 |
| Cetyl alcohol | 1.00 |
| Salicylic acid | 2.00 |
| Glycerin | 3.00 |
| Xanthan gum | 0.20 |
| Steareth-21 | 0.50 |
| Steareth-2 | 0.25 |
| Distearyldimoniumchloride | 1.50 |
| Behenyl alcohol | 0.42 |
| PPG-15 Stearyl ether (99.9%) and BHT (0.1%) | 4.00 |
| Mixture of Cetyl betaine (30%), sodium chloride (7%), alcohol (10%), water (10%) | 6.70 |
| Sodium lauryl sulphate | 3.60 |
| Polyethylene beads | 4.00 |
| Hydrolysed Milk Protein (mixed with propylene glycol and water) | 0.20 |
| Synthetic wax and mica beads | 0.35 |
| Parfum | 0.20 |
| Disodium EDTA | 0.01 |
| Aqua | to 100% |

Method

The stearyl alcohol, cetyl alcohol, behenyl alcohol, steareth-21, steareth-2, distearyldimoniumchloride, PPG-15 stearyl ether and BHT were heated to 60°C to form the oil phase. The remainder of the ingredients were mixed to form the aqueous phase. The heated oil phase was added to the aqueous phase. The composition was cooled down to room temperature with stirring.

Example 6

Gel Lotion

| Ingredients | % w/w |
|---|---|
| Alcohol (99.9%) + t-butylalcohol (0.1%) | 11.5 |
| Glycerin | 0.50 |
| Isoceteth-20 | 1.00 |
| Salicylic acid | 0.50 |
| Hydrogen peroxide (35%) | 4.29 |
| Ammonium acryloyldimethyltaurate/ vinyl pyrrolidone copolymer | 1.50 |
| Hydrolyzed Milk Protein | 0.20 |
| Sodium hydroxide (30%) | 0.40 |
| Parfum | 0.20 |
| Disodium EDTA | 0.005 |
| Aqua | to 100% |

Method

The salicylic acid was mixed into the alcohol/t-butylalcohol. When the salicylic acid was fully dissolved, the water, glycerin and disodium EDTA were mixed in. The ammonium acryloyldimethyltaurate / vinyl pyrrolidone copolymer was added with continuous homogenisation, followed by the isoceteth-20, hydrogen peroxide, hydrolysed milk peptide and parfum in the water. The pH was adjusted to pH 3 with sodium hydroxide (30%).

Example 7

Lotion

| Ingredients | % w/w |
|---|---|
| Sorbitol (70%) | 0.50 |
| Denatured ethanol | 37.00 |
| Glycerin | 1.50 |
| Isoceteth-20 | 2.00 |
| Salicylic acid | 2.00 |
| Hydrolyzed Milk Protein | 0.20 |
| Sodium hydroxide (30%) | 0.38 |
| Parfum | 0.10 |
| Aqua | to 100% |

Method

The salicylic acid, isoceteth-20 and parfum were dissolved in the ethanol to form the oil phase. The remaining ingredients were mixed with the water to form the aqueous phase. The oil and aqueous phases were mixed to form a uniform composition.

Example 8

Lotion

| Ingredients | % w/w |
|---|---|
| Sorbitol (70%) | 0.50 |
| Denatured ethanol | 37.00 |
| Hydrogen Peroxide | 4.29 |
| Isoceteth-20 | 3.00 |
| Salicylic acid | 2.00 |
| Hydrolyzed Milk Protein | 0.20 |
| Sodium hydroxide (30%) | 0.20 |
| Parfum | 0.10 |
| Disodium EDTA | 0.005 |
| Aqua | to 100% |

Method

The salicylic acid, isoceteth-20 and parfum were dissolved in the ethanol to form the oil phase. The remaining ingredients were mixed with the water to form the aqueous phase. The oil and aqueous phases were mixed to form a uniform composition.

Example 9

Clinical Trial To Determine The Influence Of Cosmetic Products Containing 2% Salicylic Acid And 0.2% Hydrolysed Milk Protein On The Sebum Level Of The Skin

Protocol

20 volunteers were included in a sebumetry study in order to evaluate the influence of several types of cosmetic formulations containing 2% salicylic acid and 0.2% HMP on the sebum level of the skin.

On the back of the volunteers, 7 areas of 5x5 cm were delimited in order to test 5 products : 3 rinse-off products (a gel wash (Example 3), a cream wash (Example 1), a cream scrub (Example 5)) and 2 leave-on products (impregnated pads (Example 4) and impregnated wipes (Example 2)).

An untreated area (used for the comparison versus leave on products) and an area washed by water and then dried (used for the comparison versus rinse-off products) was used as control. A randomisation step was used between the 7 areas on subjects in order to eliminate variations of sebum content linked with the localisation on the back.

Before any application, the sebum level was measured using a sebumeter® SM810 (Courage and Khazaka) to define baseline sebum content on each area. Other measurements were performed 2, 4 and 6 hours after the standardised application of each product on each area.

Results

The results are shown in Table 1 below.

Table 1

| | 0 hours | 2 hours | 4 hours | 6 hours |
|---|---|---|---|---|
| Untreated control | 147.8 | 153.3 | 142.7 | 141.5 |
| Gel wash | 152 | 36.3* | 45.2** | 74** |
| Cream wash | 151.9 | 33.7* | 45.7** | 72.5** |
| Cream scrub | 153.8 | 40.6* | 42.9** | 72.6** |
| Pad | 148.6 | 39* | 45.8** | 84.1 |
| Wipes | 143.7 | 45.5* | 49.3* | 78.8** |
| Water control | 156.8 | 42.5* | 114 | 140.9 |

*$p<0.05$ versus untreated value
**$p<0.05$ versus untreated and wash only value

The control area only treated with water showed statistically significant reduction only after 2 hours. Four and 6 hours after the treatment the level of sebum was not different to the untreated control.

The rinse off products (gel wash, cream wash and cream scrub) all demonstrated a statistically significant reduction of the sebum level versus water control area at two, four and six hours.

For the leave-on products, statistically significant reductions of the sebum level versus the untreated control area were found after 2, 4 and 6 hours for the impregnated wipe. Statistically significant reductions of the sebum level versus the untreated control area were found after 2 and 4 hours for the impregnated pad. The sebum quantity after 6 hours on the area treated by the pad, although being smaller, was not statistically different from the untreated area.

Conclusion

Pads showed statistically significant reduction of the sebum for at least 4 hours after use. The four other products were shown to decrease the sebum level for at least 6 hours after a single application.

Example 10

Evaluation Of Two Products Containing Salicylic Acid And Hydrolysed Milk Protein

Design

A trial was performed on different groups of 50 teenagers, of both sexes, between 12 and 19 years old suffering from impurities/spots/pimples. One of these groups tested a gel wash (Example 3) and another group tested a cream scrub (Example 5) in their normal condition of use. After 3 days use, the volunteers were contacted by phone and were asked to answer to questions regarding the safety, efficacy and cosmetic acceptability of the products. Likewise questions were asked by phone after 2 weeks use.

Results

Below is the mean of the volunteer's response to some of the questions after 3 days and 14 days use :

Regarding the Cream Scrub, 64% of the volunteers were overall very satisfied or satisfied from day 3 and even more after 14 days with 74% of the panel. This satisfaction is mainly due to better skin condition from day 3 (slightly to significantly better 64%) including pore looking smaller from Day 3 (strongly and largely agree 60%) and due to the effectiveness to combat pimples from day 3 (strongly and largely agree 68%) and to prevent from

new pimples at day 14 (strongly and largely agree 64%). Respectively 58% and 60% of the volunteers strongly or largely agree that they have less pimples and less blackheads when they use it regularly. In addition to this, their skin is softer and smoother from day 3 (strongly and largely agree respectively, 80% and 72%) and even more after 2 weeks (strongly and largely agree respectively, 86% and 80%).

This product also has a recognised action on the sebum level because 70% of the volunteers strongly and largely agree that it decreases shine after use and after 14 days, it delays the return of greasiness after application (strongly and largely agree 66%).

Regarding the Gel Wash, 69% of the volunteers were overall very satisfied or satisfied from day 3 and after 14 days with 60% of the panel. Again this satisfaction is mainly due to better skin condition from day 3 (slightly to significantly better 63%) and due to the effectiveness to combat pimples from day 3 (strongly and largely agree 63%). In addition to this, their skin is also softer and smoother from day 3 (strongly and largely agree respectively, 78% and 72%) and continues for 2 weeks (strongly and largely agree respectively, 67% and 71%). Furthermore, the product reduces skin shine right after use as assessed from day 3 (strongly and largely agree respectively, 66%) and after 14 days, it delays the return of greasiness after application (strongly and largely agree 67%).

Conclusion

Both products containing salicylic acid and HMP clearly act simultaneously:

- on sebum by showing a shine reduction and delaying the return of greasiness
- on pimples and blackheads.

These 2 products containing the active combination are clearly appreciated for their overall efficacy and their positive action on skin condition.

Claims

1. A skincare composition suitable for topical application to the skin, the composition comprising salicylic acid or a salt thereof and hydrolysed milk protein.

2. A composition as claimed in Claim 1, which comprises salicylic acid.

3. A composition as claimed in Claim 2, wherein the concentration of salicylic acid is at least 0.01% by weight, more preferably at least 0.1% by weight and most preferably at least 1% by weight.

4. A composition as claimed in Claim 2, wherein the concentration of salicylic acid is less than 10% by weight, more preferably less than 5% by weight, and most preferably less than 3% by weight.

5. A composition as claimed in Claim 2, wherein the concentration of salicylic acid is in the range from 0.01% to 10% by weight, more preferably from 0.1% to 5% by weight, and most preferably from 1% to 3% by weight.

6. A composition as claimed in Claim 1, wherein the concentration of hydrolysed milk protein is at least 0.01% by weight, more preferably at least 0.05% by weight, and most preferably at least 0.1% by weight.

7. A composition as claimed in Claim 1, wherein the concentration of hydrolysed milk protein is less than 10% by weight, more preferably less than 3% by weight, and most preferably less than 1% by weight.

8. A composition as claimed in Claim 1, wherein the concentration of hydrolysed milk protein is in the range from 0.01% to 10% by weight, more

preferably from 0.05% to 3% by weight, and most preferably from 0.1% to 1.0% by weight.

9. A composition as claimed in claim 1, wherein the concentration of salicylic acid is in the range from 0.5 to 4% by weight, more preferably from 0.5 to 2% by weight and the concentration of hydrolysed milk protein is in the range from 0.08 to 2%, more preferably from 0.1 to 0.5 % by weight.

10. A composition as claimed in any preceding claim, wherein the ratio of salicylic acid or salt thereof to hydrolysed milk protein is in the range from 1:1 to 20:1 parts by weight, more preferably from 2:1 to 15:1 parts by weight, most preferably from 5:1 to 12:1 parts by weight.

11. A composition as claimed in any preceding claim, wherein the pH of the composition is in the range from 2.3 to 7.0, more preferably from 2.5 to 6.0.

12. A composition as claimed in Claim 11, wherein the pH is in the range from 2.5 to 4.0.

13. A composition as claimed in any preceding claim further comprising one or more further topically active skincare agents selected from an anti-microbial or anti-bacterial compound, an anti-viral compound, an anti-fungal compound, an anti-inflammatory compound and an anthelmintic compound.

14. A composition as claimed in claim 13 wherein the anti-bacterial agent is a peroxide anti-bacterial agent.

15. A composition as claimed in any preceding claim, which has the form of an aqueous or oily solution or dispersion or emulsion or a gel.

16. A composition as claimed in Claim 15, which is in the form of an emulsion.

17. A composition as claimed in Claim 16, wherein the emulsion is an oil-in-water emulsion.

18. A composition as claimed in Claim 16, wherein the emulsion is a water-in-oil emulsion.

19. A composition as claimed in claim 15, which is in the form of an aqueous gel.

20. A composition as claimed in any preceding claim, which further comprises a gelling and/or a thickening agent.

21. A composition as claimed in Claim 20, wherein the gelling agent is a copolymer of acryloyl dimethyl tauric acid or a salt thereof.

22. A composition as claimed in any preceding claim, which comprises an aqueous solvent system.

23. A composition as claimed in Claim 22, wherein the solvent system is a mixed solvent system comprising water in admixture with a co-solvent.

24. A composition as claimed in Claim 23, wherein the co-solvent is an alcohol.

25. A composition as claimed in any preceding claim, which comprises one or more excipients selected from the group consisting of emulsifiers,

emollients, lipids, humectants or moisturisers, binders, conditioning agents, emulsion stabilising salts, preservatives, chelating agents or sequestering agents, abrasives, pH adjusters, surfactants, perfumes and colourings.

26. An article comprising a fibrous substrate impregnated with a skincare composition comprising salicylic acid or a salt thereof and hydrolysed milk protein.

27. An article as claimed in claim 26, wherein the fibrous material is impregnated with the skincare composition in an amount in the range from 10 to 30% by weight, preferably from 15 to 25% by weight and most preferably from 18 to 22% by weight of the fibrous material.

28. An article as claimed in either one of claims 26 or 27 comprising cellulose or cotton fibres or a mixture thereof.

29. A method for the prophylactic or remedial treatment of acne, which method comprises the topical application to the skin of a patient of a skincare composition comprising salicylic acid or a salt thereof and hydrolysed milk protein.

30. A method as claimed in Claim 29, which is a cosmetic method.

31. A method as claimed in Claim 29, which is a therapeutic method.

32. The use of salicylic acid or a salt thereof and hydrolysed milk protein in a composition for the prophylactic or remedial treatment of acne by topical application of the composition to the skin.

33. The use as claimed in claim 32 wherein salicylic acid or a salt thereof and hydrolysed milk protein are the sole active ingredients in the composition.

# INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB2005/000503

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K7/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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| X | WO 03/063816 A (THE PROCTER & GAMBLE COMPANY) 7 August 2003 (2003-08-07) | 1,2,6, 13, 15-18, 20-25, 29-33 |
| Y | page 2, last paragraph - page 3, paragraph 2<br>page 6, last paragraph - page 7, paragraph 1<br>page 10, paragraph 2<br>page 13, paragraph 1 - page 16, paragraph 2<br>claims 1-11 | 1-33 |
| | ----- | |
| | -/-- | |

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 20 July 2005 | 01/08/2005 |

| Name and mailing address of the ISA | Authorized officer |
|---|---|
| European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,<br>Fax: (+31-70) 340-3016 | Menidjel, R |

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Form PCT/ISA/210 (second sheet) (January 2004)

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International Application No
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# INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2005/000503

## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 29-33 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

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Interna[redacted]al Application No
PCT/GB2005/000503

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